3 Have Critical Care Outcomes Improved?

Emily Vail, Hayley B. Gershengorn, Hannah Wunsch

Over the past 50 years, critical care medicine has rapidly developed into a complex, resource-intensive, and multidisciplinary field. The care of patients has evolved with implementation of new monitoring devices and therapies based on the best available evidence. In addition, care has been affected by the introduction of new team members dedicated to the care of critically ill patients and specific protocols for care. In the setting of ever-changing practice, it is important to ask whether outcomes for our patients have improved.

OUTCOMES MEASURED IN CRITICALLY ILL POPULATIONS

The most consistently described outcome in both observational and interventional studies is mortality, which is variably reported as intensive care unit (ICU) mortality, in-hospital mortality, or mortality within a fixed time limit (most often between 28 and 90 days, but sometimes longer[1,2]). This chapter focuses primarily on short-term mortality, still the most commonly used measure of success.

Mortality as an outcome has the advantages of objectivity and ease of measurement, but it may not be appropriate for every study, such as in studies of palliative care when unchanged or higher mortality may be acceptable. A focus on reporting mortality can misrepresent the effect of a given intervention if the period of measurement is too short (failing to identify all related mortalities) or too long (introducing confounding from other sources of mortality). Moreover, mortality may not be the focus of an intervention or improvement initiative.

Many other endpoints have been used to assess outcome in critically ill patients (Table 3-1).[3-6] Data on these endpoints may be more difficult to obtain but may hold greater significance for patients and their caregivers. The strength of these different approaches to outcome lies in the delineation of clear administrative, policy, and economic implications and the ability to determine if these variables overlap with patient-centered outcomes (such as length of stay in the hospital).

SOURCES OF DATA

A wealth of data from various sources can be used to study critical care outcomes, including administrative data, prospectively collected clinical data, and control arms of randomized trials. Each data source has inherent strengths and weaknesses that may bias the conclusions regarding trends in mortality over time.

Administrative data are readily available from various government, public, and private sources but have important limitations. The quality of the data relies on documentation and coding by clinicians. Data acquired in this way may have low sensitivity for specific diagnoses and may be variable across individual physicians and hospitals.[7] A related concern is the potential for "upcoding," the practice of billing for more expensive diagnoses and services than provided. This (illegal) practice can create biases toward higher severity of illness.[8] Changes in coding standards or payment incentives also may alter the use of a given diagnostic code without a change in true incidence of the condition.[9,10] Finally, "extraction," the identification of certain combinations of signs, symptoms, and diagnostic terms, may be used to identify complex clinical conditions from within administrative datasets. The algorithms used in this process vary in sensitivity and specificity,[11,12] with consequences for measured incidence and outcomes.[8,12-15] Outcomes derived from administrative databases are most meaningful when their data extraction methods have been validated with multiple clinical datasets[16] and with consistent coding practices over time.

Clinical observational data can be used to study various risk factors and outcomes, but data collection is expensive and time consuming. Often, such data reflect the experience of either a single center or a few centers, and result may be poorly generalizable to other patients or institutions. Outcomes among patients randomized to receive placebo or "usual care" in controlled trials may be extrapolated to describe the natural history of a given condition. Data collected in this setting are prospective, clinically relevant, and frequently validated. However, because these patients must meet specific study inclusion criteria, they may differ significantly from the larger pool of critically ill patients with respect to severity of illness, age, comorbid disease,[17] and sites of care delivery. Moreover, such studies frequently exclude patients with poor prognoses.[18] A consistent outcome trend in all types of available data increases confidence in the conclusions drawn. When such consistency does not occur (i.e., a trend is apparent in one data type but not discernable in another), these concerns must be weighed for each study to adjudicate its quality.

Table 3-1 **Selected Common Outcome Measures for Critically Ill Patients**

Mortality	Processes of Care and Resource Use	Measures Related to Short- and Long-Term Quality of Life
ICU	ICU length of stay	ICU length of stay
Hospital	Hospital length of stay	Hospital length of stay
28 or 30 days	Time on a ventilator	Time on a ventilator
60 or more days	Ventilator-(or other) free days	Ventilator-(or other) free days
	Iatrogenic complications	Iatrogenic complications
	Location after acute hospital discharge	Location after acute hospital discharge
	Long-term health care utilization	Physical or functional disability
	Hospital costs	Hospital costs
	Hospital readmission	Hospital readmission
		Quality of dying and death
		Family satisfaction with ICU care

TRENDS IN MORTALITY

Critical care outcomes are generally studied with one of three approaches: examining outcomes among patients receiving ICU care for any reason, limiting evaluation to a specific subgroup of patients admitted to ICUs (e.g., septic shock requiring mechanical ventilation), or focusing on a specific critical illness that might necessitate admission to an ICU for a proportion of the patients (e.g., severe sepsis).

Trends for Patients Admitted to Intensive Care Units

Data showing trends over time for all ICU patients are sparse. Recent studies in which outcomes were examined over the past two decades have identified consistent changes in patient demographics and severity of illness. These differences must be accounted for when an attempt is made to determine whether outcomes have improved. A study by Zimmerman et al.[19] examined trends in in-hospital mortality among 482,601 patients admitted to U.S. ICUs between 1988 and 2012. Despite increases in severity of illness and patient age over the study period, the investigators found significant decreases in all-cause acute hospital mortality as well as in ICU and hospital lengths of stay. However, these observed improvements were partially attributable to higher rates of discharge to skilled nursing facilities. Mortality in such facilities is known to be high; therefore, although these data are clear in showing a decrease in acute hospital mortality for ICU patients over this period, we cannot conclusively determine whether overall short-term mortality decreased.

Likewise, in a retrospective analysis of a large ICU patient database in Australia and New Zealand between 2000 and 2012, Kaukonen and colleagues[20] observed decreased crude and adjusted in-hospital mortality and, with the exception of patients with severe sepsis or septic shock (who were more likely, over time, to be discharged home), increasing rates of discharge to rehabilitation facilities. In the United Kingdom, work by Hutchings et al.[21] demonstrated lower risk–adjusted ICU and hospital mortality for critically ill patients between 2000 and 2006 despite a constant severity of illness. This decrease in mortality was specifically attributed to changes in the system of care, including an increase in the number of ICU beds in the country and other systems interventions, such as critical care networks and rapid response teams.

Perhaps the most compelling evidence of improving short-term mortality for critically ill patients is the "drift" or "fade" of severity of illness scores over time.[22] Many of these scores (e.g., the Simplified Acute Physiology Score [SAPS][23] and the Acute Physiology and Chronic Health Evaluation [APACHE][24]) have been recalibrated multiple times over the past 20 to 30 years to maintain predictive accuracy. The model drift (in general) has been toward overprediction of mortality, leading to a progressive overestimation of predicted mortality that affects the accuracy of severity of illness adjustments between historical cohorts.[25] Although subtle shifts in case mix may account for some of these changes, this trend adds weight to the suggestion in the studies previously described that overall short-term mortality has decreased over time.

Trends for Specific Critical Illnesses

Changes in outcomes have been assessed for many ICU-specific illnesses. This chapter focuses on two common diagnoses: septic shock and acute respiratory distress syndrome (ARDS). A systematic review by Friedman and Vincent[26] published in 1998 examined trends in septic shock mortality with 131 studies published between 1958 and 1997. The authors found an overall mortality of 49.7%, decreasing mortality over time, and changes in infection site and causative organisms; however, they noted significant heterogeneity in definitions of disease and severity of illness between studies. Because the American College of Chest Physicians' and Society of Critical Care Medicine's 1991 European Consensus Conference definitions of sepsis, severe sepsis, and septic shock[27] have been widely adopted, comparison of outcomes over time has become a little easier, although patient populations in individual studies remain heterogeneous because of variable interpretation of aspects of the definition, such as "hypotension" and "unresponsive to adequate resuscitation."[28-30] An additional marker of possible decreasing mortality for patients with septic shock is that the mortality for the usual care arms of studies designed to capture this population has steadily decreased over time.[13]

As with septic shock, the assessment of ARDS mortality is confounded by changes in clinical definitions with time,[31,32] and trends for mortality associated with ARDS are even less consistent. A study by Milberg et al.[33] analyzed the etiology of ARDS and outcomes in the Harborview Medical Center ARDS registry and found decreases in crude and adjusted mortality between 1983 and 1993 despite increasing severity of illness. Since the publication of that study, our understanding of the pathophysiologic features of ARDS[34] and the role of ventilator-induced lung injury in patients susceptible to ARDS[35] has significantly grown. The resultant implications for ventilator management and adjunct interventions for ARDS may affect outcomes and outcomes assessment. Despite advances in understanding and options for care, recent evidence in temporal ARDS outcomes does not consistently demonstrate large improvements in mortality.

When randomized controlled trials are considered in isolation, short-term mortality among patients with ARDS does appear to be improving. Examining 2451 patients enrolled in ARDS Network randomized controlled trials, Erickson and colleagues[36] found decreased raw (from 35% to 26%) and adjusted 60-day mortality despite increased severity of illness; this trend was evident even with inclusion of patients who received high tidal volume ventilation (12 mL/kg), a finding that led the authors to conclude that observed decreases in mortality were due to generalized improvements in critical care delivery at participating hospitals rather than specific interventions for ARDS.

Two systematic reviews (incorporating both trial and observational evidence) on ARDS mortality provide conflicting results. One reported a 1.1% annual decrease in mortality[37] between 1994 (the year of publication of the European-American Consensus definitions[32]) and 2006, whereas the other found no significant change in mortality among 18,900 patients.[18] Moreover, an observational study of 514 patients with ARDS in Olmsted County, Minnesota, between 2001 and 2008 also failed to identify a significant change in hospital mortality over time.[38]

ARDS remains a heterogeneous syndrome involving subjective assessment and many causes. These inconsistencies may explain the conflicting conclusions in different studies. The development of electronic "sniffers"—programs that automatically process real-time clinical data from electronic medical records to alert clinicians to the potential presence of ARDS[39]—may provide more consistent identification of patients and thus a more accurate assessment of trends in mortality.

Trends for Diagnoses with Variable Admission to Intensive Care Units

The decision to admit a given patient to an ICU is multifactorial.[15,40,41] For example, many patients with severe sepsis are admitted to ICUs, but many patients with the same diagnosis are cared for in emergency departments,[42] hospital wards,[3,15,43,44] or step-down units.[45] Mortality in these alternative treatment sites may be substantial.[43,44]

Several large observational studies have described the epidemiologic features of severe sepsis in the United States over the past 30 years.[3,42] Serial analyses of the Agency for Healthcare Research and Quality's Nationwide Inpatient Sample (NIS) database,[46] which includes data from 1993 to 2010, demonstrate increases in measured incidence of severe sepsis and severity of illness, as well as decreased hospital mortality.[13,14,47-50] The largest of these studies, by Stevenson and colleagues,[13] included both NIS data collected between 1993 and 2009 and a meta-analysis of more than 14,000 patients enrolled in usual care or placebo arms of 36 multicenter randomized controlled trials worldwide. The authors observed differences in effect size between observational and trial data but consistent, significant decreases in overall mortality, regardless of data or the administrative coding method used. Likewise, in a study with clinical and administrative data sampled from a cohort of more than 1 million patients admitted to two U.S. medical centers between 2003 and 2012, Rhee et al.[12] found decreased hospital mortality among patients with severe sepsis.

A study of 92,000 adults with severe sepsis admitted to 240 ICUs in England, Wales, and Northern Ireland between 1996 and 2004 identified an increasing proportion of ICU admissions with sepsis. Mean patient age increased over time, but there was no change in severity of illness (as described by the APACHE II score) or the extent of organ dysfunction on admission. Importantly, unadjusted ICU and hospital mortality also were unchanged.[45] Data from Australia and New Zealand in which 100,000 ICU patients with severe sepsis were examined between 2000 and 2012 similarly showed an increasing rate of ICU admissions with severe sepsis. However, this study found decreasing rates of crude and adjusted mortality that paralleled overall ICU mortality trends and increased rates of discharge to home.[20]

The "Will Rogers phenomenon," in which earlier diagnosis of a given condition leads to an observed increase in measured incidence and decreased mortality,[51] may play a role in observed increases in severe sepsis incidence.[52] Growing clinician and hospital awareness of severe sepsis with an emphasis on early diagnosis and intervention[53] may decrease observed overall severe sepsis mortality because of the addition of a group of patients with less severe disease and lower expected mortality to a pool of previously identified, sicker patients. Appropriate risk adjustment may help to minimize this issue, but such a phenomenon remains a concern.

HAS MORTALITY IMPROVED?

Although difficult to tease apart, the trends across many, but not all, different groups of ICU patients suggest that overall short-term mortality for ICU patients has decreased over the past few decades. Observed improvements in general critical care outcomes likely reflect multiple contributing factors and may parallel improvements in overall medical care. For example, hospital mortality for *all* hospitalized patients in the United States decreased between 2000 and 2010.[54]

In the past 20 years, significant scientific progress has advanced our understanding and management of critical illness and its complications. Advances in technology and drug development and an emphasis on patient safety and quality improvement have resulted in the prevention of

complications and improved the management of comorbid diseases. Improved care of the critically ill patient likely reflects better monitoring, treatment, and overall care. However, it is also clear that improvements may not extend to all subsets of critically ill patients. Furthermore, it will be important to enhance future evaluation with the application of consistent definitions of specific disorders and with uniform practices to identify critically ill patients, irrespective of their specific diagnosis or treatment locale.

AUTHORS' RECOMMENDATIONS

Mortality associated with critical illness is challenging to accurately compare over time and between populations. To better assess outcomes and to identify potential strategies for improvement, we recommend the following:

- Awareness of the variability in diagnostic definitions and ICU admission practices that affect reported outcomes.
- Development of more precise definitions of clinical syndromes commonly observed in critically ill patients to foster standardized comparison of outcomes among patients, hospitals, and regions.
- Use of available electronic medical record abstraction systems to provide for consistent and unbiased identification of specific types of critically ill patients.

REFERENCES

1. Winters BD, et al. Long-term mortality and quality of life in sepsis: a systematic review. *Crit Care Med*. 2010;38(5):1276–1283.
2. Wunsch H, et al. Association between age and use of intensive care among surgical medicare beneficiaries. *J Crit Care*. 2013;28(5): 597–605.
3. Angus DC, et al. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. *Crit Care Med*. 2001;29(7):1303–1310.
4. Herridge MS, et al. Functional disability 5 years after acute respiratory distress syndrome. *N Engl J Med*. 2011;364(14):1293–1304.
5. DeCato TW, et al. Hospital variation and temporal trends in palliative and end-of-life care in the ICU. *Crit Care Med*. 2013;41(6): 1405–1411.
6. Kahn JM, et al. Long-term acute care hospital utilization after critical illness. *JAMA*. 2010;303(22):2253–2259.
7. Misset B, et al. Reliability of diagnostic coding in intensive care patients. *Crit Care*. 2008;12(4):R95.
8. Whittaker SA, et al. Severe sepsis cohorts derived from claims-based strategies appear to be biased toward a more severely ill patient population. *Crit Care Med*. 2013;41(4):945–953.
9. Helms CM. A pseudo-epidemic of septicemia among medicare patients in Iowa. *Am J Public Health*. 1987;77(10):1331–1332.
10. Lindenauer PK, et al. Association of diagnostic coding with trends in hospitalizations and mortality of patients with pneumonia, 2003-2009. *JAMA*. 2012;307(13):1405–1413.
11. Iwashyna TJ, et al. Identifying patients with severe sepsis using administrative claims: patient-level validation of the angus implementation of the international consensus conference definition of severe sepsis. *Med Care*. 2014;52(6):e39–43.
12. Rhee C, et al. Comparison of trends in sepsis incidence and coding using administrative claims versus objective clinical data. *Clin Infect Dis*. 2015;60(1):88–95.
13. Stevenson EK, et al. Two decades of mortality trends among patients with severe sepsis: a comparative meta-analysis. *Crit Care Med*. 2014;42(3):625–631.
14. Gaieski DF, et al. Benchmarking the incidence and mortality of severe sepsis in the United States. *Crit Care Med*. 2013;41(5): 1167–1174.
15. Sundararajan V, et al. Epidemiology of sepsis in Victoria, Australia. *Crit Care Med*. 2005;33(1):71–80.
16. Linde-Zwirble WT, Angus DC. Severe sepsis epidemiology: sampling, selection, and society. *Crit Care*. 2004;8(4):222–226.
17. Van Spall HG, et al. Eligibility criteria of randomized controlled trials published in high-impact general medical journals: a systematic sampling review. *JAMA*. 2007;297(11):1233–1240.
18. Phua J, et al. Has mortality from acute respiratory distress syndrome decreased over time?: a systematic review. *Am J Respir Crit Care Med*. 2009;179(3):220–227.
19. Zimmerman JE, Kramer AA, Knaus WA. Changes in hospital mortality for United States intensive care unit admissions from 1988 to 2012. *Crit Care*. 2013;17(2):R81.
20. Kaukonen KM, et al. Mortality related to severe sepsis and septic shock among critically ill patients in Australia and New Zealand, 2000-2012. *JAMA*. 2014;311(13):1308–1316.
21. Hutchings A, et al. Evaluation of modernisation of adult critical care services in England: time series and cost effectiveness analysis. *BMJ*. 2009;339:b4353.
22. Kramer AA. Predictive mortality models are not like fine wine. *Crit Care*. 2005;9(6):636–637.
23. Le Gall JR, Lemeshow S, Saulnier F. A new Simplified Acute Physiology Score (SAPS II) based on a European/North American multicenter study. *JAMA*. 1993;270(24):2957–2963.
24. Knaus WA, et al. The APACHE III prognostic system. Risk prediction of hospital mortality for critically ill hospitalized adults. *Chest*. 1991;100(6):1619–1636.
25. Wunsch H, Kramer AA, The role and limitation of scoring systems. In: Webb AJ, et al. ed. *Oxford Textbook of Critical Care.* Oxford University Press.
26. Friedman G, Silva E, Vincent JL. Has the mortality of septic shock changed with time. *Crit Care Med*. 1998;26(12):2078–2086.
27. Bone RC, Sibbald WJ, Sprung CL. The ACCP-SCCM consensus conference on sepsis and organ failure. *Chest*. 1992;101(6): 1481–1483.
28. Annane D, et al. Effect of treatment with low doses of hydrocortisone and fludrocortisone on mortality in patients with septic shock. *JAMA*. 2002;288(7):862–871.
29. Briegel J, et al. Stress doses of hydrocortisone reverse hyperdynamic septic shock: a prospective, randomized, double-blind, single-center study. *Crit Care Med*. 1999;27(4):723–732.
30. Sprung CL, et al. Hydrocortisone therapy for patients with septic shock. *N Engl J Med*. 2008;358(2):111–124.
31. Ranieri VM, et al. Acute respiratory distress syndrome: the Berlin definition. *JAMA*. 2012;307(23):2526–2533.
32. Bernard GR, et al. The American-European Consensus Conference on ARDS. Definitions, mechanisms, relevant outcomes, and clinical trial coordination. *Am J Respir Crit Care Med*. 1994;149(3 Pt 1): 818–824.
33. Milberg JA, et al. Improved survival of patients with acute respiratory distress syndrome (ARDS): 1983-1993. *JAMA*. 1995;273(4):306–309.
34. Matthay MA, Zimmerman GA. Acute lung injury and the acute respiratory distress syndrome: four decades of inquiry into pathogenesis and rational management. *Am J Respir Cell Mol Biol*. 2005;33(4):319–327.
35. Slutsky AS, Ranieri VM. Ventilator-induced lung injury. *N Engl J Med*. 2013;369(22):2126–2136.
36. Erickson SE, et al. Recent trends in acute lung injury mortality: 1996-2005. *Crit Care Med*. 2009;37(5):1574–1579.
37. Zambon M, Vincent JL. Mortality rates for patients with acute lung injury/ARDS have decreased over time. *Chest*. 2008;133(5): 1120–1127.
38. Li G, et al. Eight-year trend of acute respiratory distress syndrome: a population-based study in Olmsted County, Minnesota. *Am J Respir Crit Care Med*. 2011;183(1):59–66.
39. Herasevich V, et al. Validation of an electronic surveillance system for acute lung injury. *Intensive Care Med*. 2009;35(6):1018–1023.
40. Levy MM, et al. Outcomes of the Surviving Sepsis Campaign in intensive care units in the USA and Europe: a prospective cohort study. *Lancet Infect Dis*. 2012;12(12):919–924.
41. Simchen E, et al. Survival of critically ill patients hospitalized in and out of intensive care units under paucity of intensive care unit beds. *Crit Care Med*. 2004;32(8):1654–1661.

42. Wang HE, et al. National estimates of severe sepsis in United States emergency departments. *Crit Care Med*. 2007;35(8):1928–1936.
43. Esteban A, et al. Sepsis incidence and outcome: contrasting the intensive care unit with the hospital ward. *Crit Care Med*. 2007;35(5):1284–1289.
44. Sands KE, et al. Epidemiology of sepsis syndrome in 8 academic medical centers. *JAMA*. 1997;278(3):234–240.
45. Harrison DA, Welch CA, Eddleston JM. The epidemiology of severe sepsis in England, Wales and Northern Ireland, 1996 to 2004: secondary analysis of a high quality clinical database, the ICNARC Case Mix Programme Database. *Crit Care*. 2006;10(2):R42.
46. Healthcare Cost and Utilization Project. *Overview of the National (Nationwide) Inpatient Sample (NIS)*; September 11, 2014. Available from: http://www.hcup-us.ahrq.gov/nisoverview.jsp.
47. Dombrovskiy VY, et al. Rapid increase in hospitalization and mortality rates for severe sepsis in the United States: a trend analysis from 1993 to 2003. *Crit Care Med*. 2007;35(5):1244–1250.
48. Kumar G, et al. Nationwide trends of severe sepsis in the 21st century (2000-2007). *Chest*. 2011;140(5):1223–1231.
49. Lagu T, et al. What is the best method for estimating the burden of severe sepsis in the United States? *J Crit Care*. 2012;27(4):414 e1–9.
50. Gaieski DF, et al. The relationship between hospital volume and mortality in severe sepsis. *Am J Respir Crit Care Med*. 2014;190(6):665–674.
51. Feinstein AR, Sosin DM, Wells CK. The Will Rogers phenomenon. Stage migration and new diagnostic techniques as a source of misleading statistics for survival in cancer. *N Engl J Med*. 1985;312(25):1604–1608.
52. Iwashyna TJ, Angus DC. Declining case fatality rates for severe sepsis: good data bring good news with ambiguous implications. *JAMA*. 2014;311(13):1295–1297.
53. Dellinger RP, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. *Crit Care Med*. 2013;41(2):580–637.
54. Hall MJ, Levant S, DeFrances CJ. Trends in inpatient hospital deaths: National Hospital Discharge Survey, 2000-2010. *NCHS Data Brief*. 2013;118:1–8. Hyattsville, MD.